BMJ Open

The Healthy Aging and Biomarkers Cohort Study (HABCS)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-026513
Article Type:	Research
Date Submitted by the Author:	07-Sep-2018
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Keywords:	Cohort Profile, The Healthy Aging and Biomarkers Cohort Study, HABCS, Chinese oldest old

The Healthy Aging and Biomarkers Cohort Study (HABCS)

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Yue-Bin Lv and Chen Mao contributed to the work equally.

ABSTRACT

Purpose: The Chinese Longitudinal Healthy Longevity Survey Biomarkers Cohort (HABCS) was established to investigate the determinants of healthy aging and mortality among the oldest old in China. Besides collecting health status, behavioral and socio-demographic circumstances, the present study also gathers comprehensive data for the elderly by simultaneously collecting, detecting, analyzing blood and urine, respectively.

Participants: HABCS is a community-based longitudinal multi-wave study of older men and women aged 65 or above. Baseline survey and the follow-up surveys with replacement for deceased elderly were conducted in eight longevity areas in China, which cover the northern,

middle and southern parts of China. Between 2008 and 2017, 6673 participants were included in HABCS, comprising 1635 centenarians, 1564 octogenarians, 1595 nonagenarians and 1879 younger elderly (aged 65–79).

Findings to date: We have found that higher baseline total cholesterol (TC) and lipoprotein cholesterol (LDL-C) concentrations were associated with greater cognitive decline. These associations seemed to be more apparent among the centenarians, in comparison to other age groups. In addition, higher LDL-C level was associated with lower risk of all-cause mortality. There was a reverse association between plasma vitamin D and cognitive impairment in cross-sectional and prospective study.

Future plans: We are currently exploring the relationships between various biomarkers and different outcomes such as cognitive function and mortality. This longitudinal cohort study will be continued in the future.

Strengths and limitations of this study

- We select a representative sample of centenarians, nonagenarians, and octogenarians from eight longevity areas in China, which may offer a unique data set of oldest old in a non-Western country.
- Further, the HABCS provides data on under-represented age groups (e.g, centenarians), for whom comparisons often lack statistical power due to limited sample sizes in most other studies.
- Also, all the interviewees are interviewed face-to-face at home, thus limiting the underrepresentation of frailer participants

- Some limitations should be taken into considerations. Our study mainly focuses on Chinese oldest old, so our findings may not be applicable to other ethnic or age groups. And due to the special sampling design, the study population may not be a truly random sample representative of the entire population.
- Numbers of each matched age group is not as exact as we initially designed because matching eligible oldest old is difficult during field work.

INTRODUCTION

Population aging is one of the major challenges facing most countries in the world due to the declines in fertility and increases in life expectancy [1]. As for China, since the stringent implementation of population and family planning policies in the last three decades, the pace of population ageing is even more repaid than other countries. According to the 2015 census, population aged 60 and over is 222 million in China, which accounts for 16% of its total population, and by 2050 this is projected to reach 400 million or more, of which the oldest old (individuals older than 80 years) will reach 150 million. As the most rapidly growing portion of the older population [2], the oldest old is presenting a major challenge for health and social care systems because they often requires much more daily assistance and medical care [3]. Thus, it is strategically important to gain a better understanding of the determinants of healthy aging and mortality in the oldest old so to be able to reduce the negative impacts of rapid aging.

Chinese Longitudinal Healthy Longevity Survey (CLHLS) was established in China since 1998, as a sister study to other elderly cohorts (eg., HRS in the USA, SHARE in Europe, and LASI in India). The CLHLS is a community-based longitudinal cohort with the aim of examining

factors that promote longevity and quality of life among the older adults. However, we have noticed that the CLHLS study has been limited principally to social science research [3-18], whereas other objective medical aspects such as biomarkers are not available. As a result, such a major obstacle has been preventing us from developing a complete understanding of the determinants of healthy aging. Therefore, in order to address this weakness, we established a sub-cohort [The Healthy Aging and Biomarkers Cohort Study (HABCS)] in eight longevity areas from CLHLS in China in 2008. The HABCS not only covers similar domains that CLHLS has investigated, but also provides more sophisticated data for the oldest old by simultaneously collecting, detecting, analyzing blood and urine, respectively. As a result, the HABCS complements the epidemiological profile of CLHLS by examining objective biological indicators, which would provide more practical implications for the policy of health care in an ageing society.

COHORT DESCRIPTION

Participants of HABCS

HABCS is a community-based longitudinal multi-wave study of older people aged 65 or above. The baseline survey and the follow-up surveys with replacement for deceased elderly are conducted in eight longevity areas with exceptionally high densities of centenarians. These longevity areas were selected by the Chinese Society of Gerontology, which cover the northern, middle and southern parts of China. They are Laizhou City of Shandong Province, Xiayi County of Henan Province, Zhongxiang City of Hubei Province, Mayang County of Hunan Province, Yongfu County of Guangxi Autonomous Area, Sanshui District of Guangdong Province, Chengmai County of Hainan Province, and Rudong County of Jiangsu Province (Figure 1). We

interview all centenarians who voluntarily agree to participate in the baseline survey and subsequent follow-up surveys face-to-face at home, aiming to keep a large sub-sample of centenarians in the sampled longevity areas. Interviewee's age was subject to careful validation. Investigators do not ask for age directly, but verify this variable by date of birth. Further, all reported dates of birth are validated by reference to the following information: household booklet, ID card, Chinese calendar birth date and animal year, genealogical records if available, children's ages, siblings' ages, etc. As far as possible, for each centenarian interviewee, one nearby octogenarian, one nearby nonagenarian and one older adults aged 70 to 79 years old of predefined age and sex are randomly interviewed. Specifically, if the number mantissa of centenarians in the very province is between 0 and 4, one nonagenarian aged 90-94, one octogenarian aged 80-84, and one younger elderly aged 70-74 are interviewed nearby; on the other hand, if the number mantissa of centenarians is between 5 and 9, one nonagenarian aged 95-99, one octogenarian aged 85-89, and one younger elderly aged 75-79 are interviewed nearby. In addition, 0.5 nearby elderly aged 65–69 of predefined age and sex are also randomly interviewed. "Nearby" is loosely defined as in the same village or street, if available, or in the same town, same county or city. As for gender matching, if a centenarian was born in the first half of the year, corresponding matched male participants will be selected randomly. Otherwise, female participants will be selected instead. In general, we purposely try to have approximately equal numbers of male and female octogenarians and nonagenarians according to the frequency of the matched centenarians who reside nearby, and their age and sex are pre-designed based on the centenarians' code numbers (randomly assigned) and birth month.

Those interviewees who are still surviving in the follow-up waves are re-interviewed,

whereas those who are interviewed but subsequently die before the next wave will be replaced by new interviewees of the same sex and age (or within the same 5-year age group). We also try to re-interview those who lose contact previously but are still alive in the very wave. All newly-added interviewees have no kinship or family relationship with other participants.

Cohort follow-up and quality control

We included seven longevity areas for baseline survey in 2008-2009 except for Rudong County (Jiangsu Province), which was added to the survey in 2012. Follow-up surveys were carried out in 2012, 2014 and 2017 to date. In the three waves, in total, 1635, 1564, 1595, and 1879 face-to-face interviews were conducted with centenarians, nonagenarians, octogenarians, and younger elderly (aged 65–79), respectively (Table 1 shows the detailed information).

The Chinese Center for Disease Control and Prevention (CCDC) performs overall project review and validation. The provincial Disease Control and Prevention (PCDC) provide technical guidance and participate in field quality control. Health clinics in towns and townships, community health service centers and village medical personnel also involve in the research work. Fieldwork is carried out by investigators composing of 3 members, including 1 group leader (responsible for work organization and quality control), 1 interviewer (in charge of interview and filling out the questionnaires) and 1 doctor (responsible for health examination, collecting biological samples). Those who are willing to participate will sign the written informed consent. For all questions, every effort was taken to ensure the accuracy of responses: interviewers are extensively trained, and all training is standardized nationally. Detailed error checks and quality control were incorporated during the interview procedure. Blood collectors are equipped with

extensive experience in blood collection, familiar with and skilled in the use of anti-coagulation vacuum blood-collection tubes.

For the newly added participants and follow-up elderly, face-to-face interviews are performed to fill out the *Questionnaire for Interviews to the Surviving Participants* to collect their health status, behavioral and socio-demographic circumstances. Questions such as self-rated health, life satisfaction, and MMSE tests on cognitive function are answered by the interviewees only. Other questions are answered by the interviewees themselves, as much as possible. We conducted proxy interviews among the close family member for those too frail to administer questionnaires. Meanwhile, physical examination is performed, and blood as well as urine sample are also collected. For those who have died since the last follow-up, investigators would endeavour to interview their next-of-kin and complete the *Questionnaire Addressed to a Close Family Member of the Deceased*, in order to collect relevant information before the death of the participants.

The on-site chief coordinator will randomly select two questionnaires collected by each interviewer in the previous day for comprehensive review. On the other hand, the prefectural on-site chief coordinator (quality controller) also conducts a comprehensive review at the night of the visit or the next day. If problems are found, investigators should conduct a household survey or an additional telephone survey. If the telephone survey is unavailable, additional on-site investigations must be conducted. Finally, CCDC and PCDC also carry out on-site supervision and quality inspection during the investigation to ensure the process and quality of investigations.

Data Collection

Questionnaire design in HABCS is based on international standards and adapted to the

Chinese cultural context and carefully validated by pilot studies. Questions would gather information on risk factors for healthy aging and mortality, which are extremely comprehensive and are able to reflect a broad range of characteristics and conditions of the Chinese elderly. Details of the questionnaire for the surviving participants are shown in table 2. Briefly, the HABCS collects extensive information such as family structure, living arrangements, self-rated health, self-evaluation on life satisfaction, chronic disease, medical care, social activities, diet, smoking and alcohol drinking, psychological characteristics, economic resources, caregiver and family support, nutrition and some health-related conditions in early life. Activities of Daily Living (ADL) and cognitive function confirmed by the Mini-Mental State Examination (MMSE) are also evaluated. As for those who have died before the next wave, investigators will interview one of their next-of-kin. The collected information before dying includes date/cause of death, chronic diseases, ADL, number of hospitalizations or incidents of being bedridden from the last interview to death, and whether the participants have been able to obtain adequate medical treatment when suffering from disease. We also collect information on socioeconomic and demographic characteristics, such as marital status, family structure, caregivers, financial situation, and living arrangement before death. In addition to administering structured questionnaires, physical examination is conducted, including blood pressure, heart rate, rhythm, height, weight, waist circumference, hip circumference, the ability to move physically, the ability to pick up ground books, number of steps needed to rotate one circle, respiratory function, grip force, nerves, hearing, chest, abdominal, and language. Meanwhile, fasting blood samples as well as urine for biomarker measurements are collected. For all the interviewees, we collect 7ml venous blood sample (5ml+2ml) in total with two heparin anticoagulation blood collection tubes. One of the

tubes with 5 ml blood sample is centrifuged to obtain plasma and blood cells, after which 1.0-1.2 ml of plasma is separately stored into two freezing tubes, whereas white blood cells layer is absorbed and stored in the other tube. The remaining 2 ml blood sample is stored into 2 freezing tube, with 1 ml blood for each for further analyzing. Besides, 50ml urine sample is collected. Specifically, 2ml urine sample is stored into a freezing tube, while the remaining sample is stored into the other freezing tubes, with each tube storing 4.5ml urine sample, resulting in 9 tubes totally. Finally, the left urine sample is used for on-site creatinine detection. After on-site investigations, all plasma, white blood cells, whole blood, and urine samples are stored in transport cases provided by CCDC and transported at -20℃ by specially-assigned persons to designated testing units. A variety of biological indicators are analyzed (Table 3). All laboratory analyses are conducted by the central clinical lab at Capital Medical University in Beijing.

Patient and Public Involvement

None of the participants was involved in the questionnaire design, biological measurements, or outcome measures; they were likewise not involved in the design, recruitment, and implementation of the study. Furthermore, all participants or their relatives were informed of the use of the data for research in this study. There were no plans to disseminate the study results to participants.

FINDINGS TO DATE

Recent publications of this cohort were focused on links between biomarkers and mortality or cognitive impairment. Details of the findings are shown as follows:

Lipid and cognitive function

We have shown that higher baseline total cholesterol (TC) and lipoprotein cholesterol (LDL-C) concentrations were associated with greater cognitive decline [19]. Compared with the lowest quartiles, the corresponding adjusted mean differences in cognitive decline rate for TC and LDL-C were 0.28 points (MMSE score) per year [95% confident interval (CI): -0.54, –0.02; *P* for trend = 0.005] and 0.42 points per year (95% CI: -0.69, -0.16; *P* for trend = 0.006), respectively. Further, the associations between all lipids and cognitive decline appeared to be more pronounced among the centenarians, in comparison to other age groups.

Lipid and all-cause mortality

HABCS has also observed that higher LDL-C level was associated with lower risk of all-cause mortality [20]. Our results indicated that each 1 mmol/L increase of LDL-C concentration resulted in a 19% decrease in 3-year all-cause mortality [hazard ratio (HR): 0.81, 95% CI: 0.71-0.92]. The adjusted HR for abnormally higher LDL-C concentration (≥3.37 mmol/L) was 0.60 (95% CI: 0.37-0.95) compared with the low LDL-C concentration. This is the first study using a relatively large sample of oldest old to investigate the associations between LDL-C and all-cause mortality.

Vitamin D levels and cognitive function

We have examined the cross-sectional association between quartiles of plasma vitamin D level and cognitive impairment (MMSE score <18) by using logistic regressions. There was a reverse association between plasma vitamin D and cognitive impairment after adjusting for various covariates. The multivariable adjusted odds ratio for lowest versus highest plasma vitamin

D quartiles was 2.15 (95% CI: 1.05–4.41) for cognitive impairment, and the multivariable odds ratio associated with 1-SD decrement of plasma vitamin D was 1.32 (95% CI: 1.00–1.74) for cognitive impairment. Subgroup analyses have indicated that these associations did not vary significantly between gender and different age groups (all *P* for interaction > 0.05). This study used the largest sample size of oldest old in Asia to explore relationship between plasma vitamin D and cognitive impairment [21].

Meanwhile, we have also investigated prospective associations between vitamin D levels at baseline and risk of subsequent cognitive decline and impairment. Participants with lower plasma vitamin D levels had a higher risk of a decrease of ≥ 3 MMSE points over the 2-year follow-up in comparison to those with higher levels. The fully-adjusted OR associated with 1-SD decrement of plasma vitamin D levels was 1.35 (95% CI: 1.10-1.66) for cognitive decline. These results were not gender specific [22].

STRENGTHS AND LIMITATIONS

As for strengths, we select a representative sample of centenarians, nonagenarians, and octogenarians from eight longevity areas through a resemble case-control design, which may offer a unique data set of oldest old in a non-Western country. Further, the HABCS provides data on under-represented age groups (e.g, centenarians), for whom comparisons often lack statistical power due to limited sample sizes. Also, all the interviewees are interviewed face-to-face at home, thus limiting the underrepresentation of frailer participants. Another key strength is that, the field and research teams have extensive experience implementing fieldwork, and a variety of grass-roots health institutions have participated in the project, with the CCDC and

PCDC providing project review and validation as well as technical guidance. This multi-collaboration system would insure the quality of our research. In addition, most of the variables were repeatedly collected through multiple waves, which would facilitate the tracing of trajectories of healthy ageing. Besides, all laboratory analyses were centrally conducted by a central clinical lab at Capital Medical University, which is equipped with requisite skills and facilities, thereby eliminating inter-laboratory assay. More importantly, we collect comprehensive data by including a broad range of variables especially biological indicators, all of which will allow meaningful adjustment of various confounders when dissecting the complex inter-relationships of factors and identifying modifiable risk factors and biomarkers for healthy aging. Last but not least, the interview refusal rate among the Chinese oldest old was very low: about 2 percent among those who were not too sick to participate with proxy assistance.

Several limitations should be taken into consideration: 1) our study mainly focuses on Chinese oldest old, so our findings may not be applicable to other ethnic or age groups. 2) Due to the special sampling design, the study population may not be a truly random sample representative of the entire population. 3) The relative high rate of lost to follow-up due to the old age and low education status of our participants may bring bias. 4) Numbers of each matched age group is not as exact as we initially designed because matching eligible oldest old is difficult during field work. 5) One would argue that attrition from wave to wave is inherent in most longitudinal studies of elderly, which would result in positive selection effects. However, we try to re-interview all of the elderly who are lost to follow-up in each wave and replace for the deceased elderly, through which the sample size would be relatively stable over time.

COLLABORATION

The data of HABCS are publicly available. More details about HABCS are available on the website: www.habcs.cn. We welcome joint analyses of the cohort data. Any research group can submit a research proposal providing information on background, research questions, methods, timetable and budget as well as authorship for new collaborations. Research proposals will be reviewed by scientific committee.

FUNDING

The HABCS is jointly supported by National Natural Sciences Foundation of China (grant number 71233001, 71490732 to Y.Z. and 81273160, 81573247 to X.M.S.), the U.S. National Institute of Aging (grant number 2P01AG031719 to Y.Z.) and United Nations Fund for Population Activities, and a Claude D. Pepper Older Americans Independence Centers grant (5P30AG028716 from NIA to VBK).

ACKNOWLEDGEMENTS

We thank the patients who contributed to this cohort

CONTRIBUTORS

The study protocol was designed by X.-M. Shi. Y.-B. Lv and C. Mao drafted the manuscript. Z.-X. Yin, F.-R. Li and X.-B. Wu performed the data quality control and the statistical analysis. All authors participated in the study design, revised the article and approved the final version.

COMPETING INTERESTS STATEMENT

None declared

Table 1. Age and sex compositions of the samples of the baseline survey and subsequent follow-up in HABCS.

Age group	Surviving interviewees									Deceased interviewees		
	Newly added			Follow-up			Total					
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
2008-2009 baseline	1312	1772	3084	-	-	-	1312	1772	3084	-	-	-
centenarian	91	587	678	-	-	-	91	587	678	-	-	-
nonagenarian	270	460	730	-	-	-	270	460	730	-	-	-
octogenarian	414	399	813	-	-	-	414	399	813	-	-	-
Younger elderly	537	326	863	-	-	-	537	326	863	-	-	-
2012 follow-up	518	737	1255	1165	1545	2710	1683	2282	3965	377	706	1083
centenarian	62	354	416	85	520	605	147	874	1021	61	376	437
nonagenarian	96	140	236	243	400	643	339	540	879	144	219	363
octogenarian	147	133	280	362	341	703	509	474	983	122	87	209
Younger elderly	213	110	323	475	284	759	688	394	1082	50	24	74
2014 follow-up	390	530	920	1651	2,307	3958	2041	2837	4878	380	310	690
centenarian	34	171	205	142	876	1018	176	1,047	1223	107	154	261
nonagenarian	124	167	291	344	559	903	468	726	1194	90	113	203
octogenarian	116	137	253	517	485	1002	633	622	1255	104	61	165
Younger elderly	116	55	171	648	387	1035	764	442	1206	41	20	61
2017 follow-up	601	813	1414	1026	1,285	2311	1627	2098	3725	309	532	841
centenarian	58	278	336	77	383	460	135	661	796	57	269	326
nonagenarian	151	156	307	222	329	551	373	485	858	120	166	286
octogenarian	127	122	249	298	336	634	425	458	883	91	83	174
Younger elderly	265	257	522	429	237	666	694	494	1188	41	14	55

Table 2. Data Collection from *Questionnaire for Interviews to the Surviving Participants* in HABCS.

Questionnaire for Interviews to the Surviving Participants in HABCS		
Basic Information	**Life Evaluation and Personality**	**Mini Mental State Examination (MMSE)**
Sex Ethnic group Age Place of Birth Characteristics of Current Residence	Life Satisfaction and Self-Rated Health Personality	Orientation Registration Attention and Calculation Recall Language
Life Style	**Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL)**	**Personal Background**
Diet Smoke 1.Tobacco-Nicotine Dependence 2.Personal Perception and Knowledge of Smoking-related Cancer Risk 3.Passive Smoke Exposure Alcohol Alcohol - Lifetime Abuse and Dependence Exercises Physical Activity Other Activities	Limited in Activities ADL Bathing Dressing Toilet Indoor Transfer Continence Eating Characteristics of Caregiver IADL	Education Primary Occupation before age 60 Retirement Age Pension for Retirement Public Old Age Insurance Financial Support Economic Status Current Marital Status Medical Service Social Security and Commercialized Insurances Childhood status Mother's Information Father's Information Birth Order Biological Brothers' and Sisters' Information Children's Information Money Gotten/Given Social Services in The Living Community Preference of Living Arrangement
Objective Examination and Illnesses Attention		
Sleep Quality Teeth Status		

Oral Hygiene of Personal Care
Toothache and Orofacial Pain
Hand Dominance
Standing Height or
Self-Reported Height
Waist Circumference
Hearing loss
Physical Illnesses

Table 3. Biological samples tested in HABCS.

Biological Samples	**Specific Biological Indicators Tested**
Blood Routine Examination	Blood platelet, Hemoglobin, Red Blood Cell, White blood cell
Urine Routine Examination	Bilirubin, Creatinine, Erythrocyte, Glucose, Ketone body, Leukocyte, Microalbuminuria, Nitrite, Occult blood, Specific gravity, Urine protein, Urobilinogen, pH,
Blood Biochemistry	Fasting blood-glucose, Glycated albumin, High-density lipoprotein, High-sensitivity C-reactive protein, Low density lipoprotein, Malondialdehyde, Plasma albumin, Serum creatinine, Superoxide dismutase, Total cholesterol, Triglyceride, Uric acid, Urea nitrogen, 25-Hydroxyvitamin D

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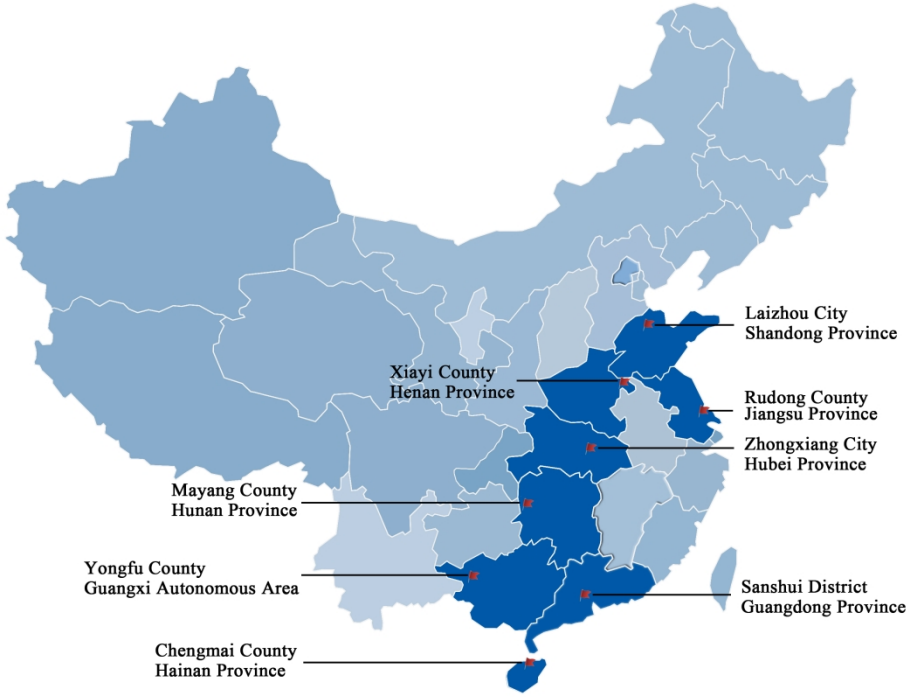

Figure 1. Selected longevity areas in China for sampling in HABCS.

1058x811mm (72 x 72 DPI)

BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-026513.R1
Article Type:	Cohort profile
Date Submitted by the Author:	02-Apr-2019
Complete List of Authors:	Lv, Yue-Bin; Chinese Center for Disease Control and Prevention, National Institute of Environmental Health Mao, Chen; School of Public Health, Southern Medical University, Department of Epidemiology Yin, Zhaoxue Li, Fu-Rong; Southern Medical University, Division of Epidemiology Wu, Xian-Bo; Southern Medical University, Division of Epidemiology Shi, Xiaoming; Chinese Center for Disease Control and Prevention, National Institute of Environmental Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Epidemiology, Geriatric medicine, Health policy
Keywords:	Cohort Profile, The Healthy Aging and Biomarkers Cohort Study, HABCS, Chinese oldest old

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Yue-Bin Lv and Chen Mao contributed to the work equally.

ABSTRACT

Purpose: The Chinese Longitudinal Healthy Longevity Survey Biomarkers Cohort (HABCS) was established to investigate the determinants of healthy aging and mortality among the oldest old in China. Besides collecting health status, behavioral and socio-demographic circumstances, the present study also gathers comprehensive data for the elderly by simultaneously collecting, detecting, analyzing blood and urine, respectively.

Participants: HABCS is a community-based longitudinal multi-wave study of older men and women aged 65 or above. Baseline survey and the follow-up surveys with replacement for

deceased elderly were conducted in eight longevity areas in China, which cover the northern, middle and southern parts of China. Between 2008 and 2017, 6673 participants were included in HABCS, comprising 1635 centenarians, 1595 nonagenarians, 1564 octogenarians and 1879 younger elderly (aged 65–79).

Findings to date: We have found that higher baseline levels of 1) total cholesterol (TC) , 2) lipoprotein cholesterol (LDL-C) and 3) superoxide dismutase activity were associated with greater cognitive decline. In addition, 4) higher LDL-C level was associated with lower risk of all-cause mortality. There was a reverse association between 5) plasma vitamin D and cognitive impairment in cross-sectional and prospective study.

Future plans: We are currently exploring the relationships between various biomarkers and different outcomes such as cognitive function and mortality. This longitudinal cohort study will be continued in the future.

Strengths and limitations of this study

- We select a representative sample of centenarians, nonagenarians, and octogenarians from eight longevity areas in China, which may offer a unique data set of oldest old in a non-Western country.
- The HABCS provides data on under-represented age groups (e.g, centenarians), for whom comparisons often lack statistical power due to limited sample sizes in most other studies.
- All the interviewees are interviewed face-to-face at home, thus limiting the underrepresentation of frailer participants
- This study mainly focuses on Chinese oldest old, so the findings may not be applicable to

other ethnic or age groups.

- Due to the special sampling design, the study population may not be a truly random sample representative of the entire population.

INTRODUCTION

Population aging is one of the major challenges facing most countries in the world due to the declines in fertility and increases in life expectancy [1]. As for China, since the stringent implementation of population and family planning policies in the last three decades, the pace of population ageing is even more rapid than other countries. According to the 2015 census, population aged 60 and over is 222 million in China, which accounts for 16% of its total population, and by 2050 this is projected to reach 400 million or more, of which the oldest old (individuals older than 80 years) will reach 150 million. As the most rapidly growing portion of the older population [2], the oldest old is presenting a major challenge for health and social care systems because they often require much more daily assistance and medical care [3]. Thus, it is strategically important to gain a better understanding of the determinants of healthy aging and mortality in the oldest old so to be able to reduce the negative impacts of rapid aging.

Chinese Longitudinal Healthy Longevity Survey (CLHLS) was established in China since 1998, as a sister study to other elderly cohorts (eg., the Health and Retirement Study (HRS) in the USA, the Survey of Health, Ageing and Retirement (SHARE) in Europe, and Longitudinal Aging Study in India (LASI)). The CLHLS is a community-based longitudinal cohort with the aim of examining factors that promote longevity and quality of life among the older adults. However, we have noticed that the CLHLS study has been limited principally to social science research [3-18],

whereas other objective medical aspects such as biomarkers are not available. As a result, such a major obstacle has been preventing us from developing a complete understanding of the determinants of healthy aging. Therefore, in order to address this weakness, we established a sub-cohort [The Healthy Aging and Biomarkers Cohort Study (HABCS)] in eight longevity areas from CLHLS in China in 2008. The HABCS not only covers similar domains that CLHLS has investigated, but also provides more sophisticated data for the oldest old by simultaneously collecting, detecting, analyzing blood and urine, respectively. As a result, the HABCS complements the epidemiological profile of CLHLS by examining objective biological indicators, which would provide more practical implications for the policy of health care in an ageing society.

COHORT DESCRIPTION

Participants of HABCS

HABCS is a community-based longitudinal multi-wave study of older people aged 65 or above. The baseline survey and the follow-up surveys with replacement for deceased elderly are conducted in eight longevity areas with exceptionally high densities of centenarians. These longevity areas were selected by the Chinese Society of Gerontology, which cover the northern, middle and southern parts of China. They are Laizhou City of Shandong Province, Xiayi County of Henan Province, Zhongxiang City of Hubei Province, Mayang County of Hunan Province, Yongfu County of Guangxi Autonomous Area, Sanshui District of Guangdong Province, Chengmai County of Hainan Province, and Rudong County of Jiangsu Province [19] (Figure 1). We interview all centenarians who voluntarily agree to participate in the baseline survey and subsequent follow-up surveys face-to-face at home, aiming to keep a large sub-sample of

centenarians in the sampled longevity areas. Interviewee's age was subject to careful validation. Investigators do not ask for age directly, but verify this variable by date of birth. Further, all reported dates of birth are validated by reference to the following information: household booklet, ID card, Chinese calendar birth date and animal year, genealogical records if available, children's ages, siblings' ages, etc [20]. As far as possible, for each centenarian interviewee, one nearby octogenarian, one nearby nonagenarian and one older adults aged 70 to 79 years old of predefined age and sex are randomly interviewed. Specifically, if the number mantissa of centenarians in the very province is between 0 and 4, one nonagenarian aged 90-94, one octogenarian aged 80-84, and one younger elderly aged 70-74 are interviewed nearby; on the other hand, if the number mantissa of centenarians is between 5 and 9, one nonagenarian aged 95-99, one octogenarian aged 85-89, and one younger elderly aged 75-79 are interviewed nearby. In addition, 0.5 nearby elderly aged 65–69 of predefined age and sex are also randomly interviewed. "Nearby" is loosely defined as in the same village or street, if available, or in the same town, same county or city [21]. As for gender matching, if a centenarian was born in the first half of the year, corresponding matched male participants will be selected randomly. Otherwise, female participants will be selected instead (Figure 2). In general, women had a larger proportion in comparison to men among the oldest old, thus we purposely try to have approximately equal numbers of male and female octogenarians and nonagenarians according to the frequency of the matched centenarians who reside nearby, and their age and sex are pre-designed based on the centenarians' code numbers (randomly assigned) and birth month.

Those interviewees who are still surviving in the follow-up waves are re-interviewed, whereas those who are interviewed but subsequently die before the next wave will be replaced by

new interviewees of the same sex and age (or within the same 5-year age group). We also try to re-interview those who lose contact previously but are still alive. All newly-added interviewees have no kinship or family relationship with other participants [20].

Cohort follow-up and quality control

We included seven longevity areas for baseline survey in 2008-2009 except for Rudong County (Jiangsu Province), which was added to the survey in 2012. Follow-up surveys were carried out in 2012, 2014 and 2017 to date. In the three waves, in total, 1635, 1564, 1595, and 1879 face-to-face interviews were conducted with centenarians, nonagenarians, octogenarians, and younger elderly (aged 65–79), respectively (Table 1 and Table 2 show the detailed information).

The Chinese Center for Disease Control and Prevention (CCDC) performs overall project review and validation. The provincial Disease Control and Prevention (PCDC) provide technical guidance and participate in field quality control. Health clinics in towns and townships, community health service centers and village medical personnel also involve in the research work. Fieldwork is carried out by investigators composing of 3 members, including 1 group leader (responsible for work organization and quality control), 1 interviewer (in charge of interview and filling out the questionnaires) and 1 doctor (responsible for health examination, collecting biological samples). Those who are willing to participate will sign the written informed consent. Participants would receive incentives for delaying his/her work by the interview. Incentives are gifts that are worth no more than ¥30. For all questions, every effort was taken to ensure the accuracy of responses: interviewers are extensively trained, and all training is standardized nationally. Detailed error checks and quality control were incorporated during the interview

procedure. Participants were informed in advance the designated times when the research teams would visit, and the blood was collected after an overnight fast. Blood collectors are equipped with extensive experience in blood collection, familiar with and skilled in the use of anti-coagulation vacuum blood-collection tubes.

For the newly added participants and follow-up elderly, face-to-face interviews are performed to fill out the *Questionnaire for Interviews to the Surviving Participants* to collect their health status, behavioral and socio-demographic circumstances. Questions such as self-rated health, life satisfaction, and MMSE tests on cognitive function are answered by the interviewees only. Other questions are answered by the interviewees themselves, as much as possible. We conducted proxy interviews among the close family member for those too frail to administer questionnaires. Meanwhile, physical examination is performed, and blood as well as urine sample are also collected. For those who have died since the last follow-up, investigators would endeavour to interview their next-of-kin and complete the *Questionnaire Addressed to a Close Family Member of the Deceased*, in order to collect relevant information before the death of the participants.

The on-site chief coordinator will randomly select two questionnaires collected by each interviewer in the previous day for comprehensive review. On the other hand, the prefectural on-site chief coordinator (quality controller) also conducts a comprehensive review at the night of the visit or the next day. If problems are found, investigators should conduct a household survey or an additional telephone survey. If the telephone survey is unavailable, additional on-site investigations must be conducted. Finally, CCDC and PCDC also carry out on-site supervision and quality inspection during the investigation to ensure the process and quality of investigations.

Data Collection

Questionnaire design in HABCS is based on international standards and adapted to the Chinese cultural context and carefully validated by pilot studies [20]. Questions would gather information on risk factors for healthy aging and mortality, which are extremely comprehensive and are able to reflect a broad range of characteristics and conditions of the Chinese elderly. Details of the questionnaire for the surviving participants are shown in table 3. Briefly, by using questionnaires, the HABCS collects extensive information such as family structure, living arrangements, self-rated health, self-evaluation on life satisfaction, chronic disease, medical care, social activities, diet, smoking and alcohol drinking, psychological characteristics, economic resources, caregiver and family support, nutrition and some health-related conditions in early life [3]. Activities of Daily Living (ADL) and cognitive function confirmed by the Mini-Mental State Examination (MMSE) are also evaluated [22, 23]. We documented the date of death from the family members of the deceased or local doctors. As for those who have died before the next wave, investigators will interview one of their next-of-kin. The collected information before dying includes date/cause of death, chronic diseases, ADL, number of hospitalizations or incidents of being bedridden from the last interview to death, and whether the participants have been able to obtain adequate medical treatment when suffering from disease. We also collect information on socioeconomic and demographic characteristics, such as marital status, family structure, caregivers, financial situation, and living arrangement before death. In addition to administering structured questionnaires, physical examination is conducted, including blood pressure, heart rate, rhythm, height, weight, waist circumference, hip circumference, the ability to move physically, the

ability to pick up ground books, number of steps needed to rotate one circle, respiratory function, grip force, nerves, hearing, chest, abdominal, and language. Meanwhile, fasting blood samples as well as urine for biomarker measurements are collected. Blood samples were collected after an overnight fast (more than 12-hours). For all the interviewees, we collect 7ml venous blood sample (5ml+2ml) in total with two heparin anticoagulation blood collection tubes. One of the tubes with 5 ml blood sample is centrifuged to obtain plasma and blood cells, after which 1.0-1.2 ml of plasma is separately stored into two freezing tubes, whereas white blood cells layer is absorbed and stored in the other tube. The remaining 2 ml blood sample is stored into 2 freezing tube, with 1 ml blood for each for further analyzing. Additionally, 50ml urine sample is collected after an overnight fast (more than 12-hours). Specifically, 2ml urine sample is stored into a freezing tube, while the remaining sample is stored into the other freezing tubes, with each tube storing 4.5ml urine sample, resulting in 9 tubes in total. Finally, the remaining urine sample is used for on-site creatinine detection. During on-site investigations, blood samples were centrifuged within one hour after blood collection for the separation of plasma from blood cell. Heparin anticoagulant blood samples were centrifuged at 3000 rpm for 10 minutes at 18-25 °C. Then all plasma, white blood cells, whole blood, and urine samples are stored at -80℃ in the county CDC. And then the sample were transported at -20℃ with transport cases provided by CCDC by specially-assigned persons to designated testing units. After the plasma vs blood separation, natural sinking method was used to isolate white blood cells from red blood cells. We have added this information to the revised manuscript.. A variety of biological indicators are analyzed (Table 4). All laboratory analyses are conducted by the central clinical lab at Capital Medical University in Beijing. Laboratory quality control material was run at the beginning of

each shift. Levey–Jennings chart was plotted on to give a visual indication whether a laboratory test is working well. A mark is made indicating how far away the actual result was from the mean (which is the expected value for the control). Lines run across the graph at the mean, as well as one, two and three standard deviations to either side of the mean. This makes it easy to see how far off the result was. The freeze thaw only occurred once from the collection of biological samples to the determination of biomarkers.

Patient and Public Involvement

None of the participants was involved in the questionnaire design, biological measurements, or outcome measures; they were likewise not involved in the design, recruitment, and implementation of the study. Furthermore, all participants or their relatives were informed of the use of the data for research in this study. There were no plans to disseminate the study results to participants.

FINDINGS TO DATE

As HABCS was established to investigate the determinants of healthy aging. The biomarkers we focused on are either the confounding factors or the risk factors for adverse health outcomes in the older adults. In fact, recent publications of this cohort have reported links between biomarkers and mortality or cognitive impairment. Details of the findings are shown as follows:

Lipid and cognitive function

We have shown that higher baseline total cholesterol (TC) and lipoprotein cholesterol

(LDL-C) concentrations were associated with greater cognitive decline [24]. Compared with the lowest quartiles, the corresponding adjusted mean differences in cognitive decline rate for TC and LDL-C were 0.28 [95% confident interval (CI): -0.54, –0.02; *P* for trend = 0.005] and 0.42 (95% CI: -0.69, -0.16; *P* for trend = 0.006), respectively. Further, the associations between all lipids and cognitive decline appeared to be more pronounced among the centenarians, in comparison to other age groups. It should be cautious that these findings were not accounted for competing risks and potential reverse causation should also be taken into account due to the short follow-up period.

Lipid and all-cause mortality

HABCS has also observed that higher LDL-C level was associated with lower risk of all-cause mortality [25]. Our results indicated that each 1 mmol/L increase of LDL-C concentration resulted in a 19% decrease in 3-year all-cause mortality [hazard ratio (HR): 0.81, 95% CI: 0.71-0.92]. The adjusted HR for abnormally higher LDL-C concentration (≥3.37 mmol/L) was 0.60 (95% CI: 0.37-0.95) compared with the low LDL-C concentration. This is the first study to investigate this association in a non-Western population. However, potential reverse causation might have affected the associations found..

Vitamin D levels and cognitive function

We have examined the cross-sectional association between quartiles of plasma vitamin D level and cognitive impairment (MMSE score <18) by using logistic regressions [26]. Adjustments were made for demographics, diseases and various biomarkers. After adjusting for various covariates, there was a reverse association between plasma vitamin D and cognitive impairment. . The multivariable adjusted odds ratio for lowest versus highest plasma vitamin D quartiles was

2.15 (95% CI: 1.05–4.41) for cognitive impairment, and the multivariable odds ratio associated with 1-SD decrement of plasma vitamin D was 1.32 (95% CI: 1.00–1.74) for cognitive impairment. Subgroup analyses have indicated that these associations did not vary significantly between gender and different age groups (all *P* for interaction > 0.05). This study used the largest sample size of oldest old in Asia to explore relationship between plasma vitamin D and cognitive impairment.

Meanwhile, we have also investigated prospective associations between vitamin D levels at baseline and risk of subsequent cognitive decline and impairment [19]. Participants with lower plasma vitamin D levels had a higher risk of a decrease of ≥ 3 MMSE points over the 2-year follow-up in comparison to those with higher levels. The fully-adjusted OR associated with 1-SD decrement of plasma vitamin D levels was 1.35 (95% CI: 1.10-1.66) for cognitive decline. These results were not gender specific. Given the short follow-up period and high mortality rate, the reverse causation among this study population and the absence of accounting for competing risks from morality restricts interpretation of this results.

Superoxide dismutase activity and cognitive function

Researchers have also examined the association between plasma superoxide dismutase (SOD) activity and cognitive decline in HABCS [27]. Participants in the highest quartile of SOD activity had an increased risk of cognitive decline in comparison to those in the lowest quartile (relative risk [RR]= 1.32, 95% CI: 1.00–1.74, P = 0.051).Using cut-off points determined by Chi-square automatic interaction detector analysis (CHAID), the multivariable relative risks (RRs; 95% CI) for the lowest category, second highest, and the highest versus the third highest category

of SOD activity were 0.56 (0.34–0.92), 1.26 (1.03–1.54), and 0.96 (0.70–1.31), respectively. This study indicated that a higher SOD activity was associated with elevated risk of cognitive decline among Chinese older adults. These results were generally consistent after accounting for competing risks from mortality. However, reverse causation should be taken into account giving the relatively short follow-up period.

STRENGTHS AND LIMITATIONS

As for strengths, we select a representative sample of centenarians, nonagenarians, and octogenarians from eight longevity areas through a special design that resembles a case-control design, which may offer a unique data set of oldest old in a non-Western country. Further, the HABCS provides data on under-represented age groups (e.g, centenarians), for whom comparisons often lack statistical power due to limited sample sizes. Also, all the interviewees are interviewed face-to-face at home, thus limiting the underrepresentation of frailer participants. Another key strength is that, the field and research teams have extensive experience implementing fieldwork, and a variety of health care facilities have participated in the project, with the CCDC and PCDC providing project review and validation as well as technical guidance. This multi-collaboration system would insure the quality of our research. In addition, most of the variables were repeatedly collected through multiple waves, which would facilitate the tracing of trajectories of healthy ageing. Besides, all laboratory analyses were centrally conducted by a central clinical lab at Capital Medical University, which is equipped with requisite skills and facilities, thereby eliminating inter-laboratory assay. More importantly, we collect comprehensive data by including a broad range of variables especially biological indicators, all of which will

allow meaningful adjustment of various confounders when dissecting the complex inter-relationships of factors and identifying modifiable risk factors and biomarkers for healthy aging. Last but not least, the interview refusal rate among the Chinese oldest old was very low: about 2 percent among those who were not too sick to participate with proxy assistance.

Several limitations should be taken into consideration: 1) our study mainly focuses on Chinese oldest old, so our findings may not be applicable to other ethnic or age groups. 2) The areas (including Rudong County) we selected have higher densities of centenarians and higher life expectancies, this may partly due to the special environmental influences plus socio-economic factors. Thus HABCS may not be representative of the general population in China. 3) The relative high rate of lost to follow-up due to the old age and low education status of our participants may bring bias. 4) Numbers of each matched age group is not as exact as we initially designed because matching eligible oldest old is difficult during field work. 5) One would argue that attrition from wave to wave is inherent in most longitudinal studies of elderly, which would result in positive selection effects. However, we try to re-interview all of the elderly who are lost to follow-up in each wave and replace for the deceased elderly, through which the sample size would be relatively stable over time.

Figure legends

Figure 1. Selected longevity areas in China for sampling in HABCS.

Figure 2. Matched-recruitment procedure of gender for a centenarian.

DATA AVAILABILITY STATEMENT

The data of HABCS are publicly available. More details about HABCS are available on the website: (http://www.habcs.cn/). We welcome joint analyses of the cohort data. Any research group can submit a research proposal providing information on background, research questions, methods, timetable and budget as well as authorship for new collaborations. Research proposals will be reviewed by scientific committee.

FUNDING

The HABCS is jointly supported by National Natural Sciences Foundation of China (grant number 71233001, 71490732 to Y.Z. and 81273160, 81573247 to X.M.S.), the U.S. National Institute of Aging (grant number 2P01AG031719 to Y.Z.) and United Nations Fund for Population Activities, and a Claude D. Pepper Older Americans Independence Centers grant (5P30AG028716 from NIA to VBK).

ACKNOWLEDGEMENTS

We thank the patients who contributed to this cohort

CONTRIBUTORS

The study protocol was designed by X.-M. Shi. Y.-B. Lv and C. Mao drafted the manuscript. Z.-X. Yin, F.-R. Li and X.-B. Wu performed the data quality control and the statistical analysis. All authors participated in the study design, revised the article and approved the final version.

COMPETING INTERESTS STATEMENT

None declared

ETHICS APPROVAL

The study was approved by the biomedical ethics committee of Peking University and Duke University

Table 1. Age and sex compositions of the samples of the baseline survey and subsequent follow-up in HABCS.

Age group	Surviving interviewees									Deceased interviewees		
	Newly added			Follow-up			Total					
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
2008-2009 baseline	1312 (42.54%)	1772 (57.46%)	3084 (100%)	-	-	-	1312 (42.54%)	1772 (57.46%)	3084	-	-	-
centenarian	91 (13.42%)	587 (86.58%)	678 (100%)	-	-	-	91 (13.42%)	587 (86.58%)	678	-	-	-
nonagenarian	270 (36.99%)	460 (63.01%)	730 (100%)	-	-	-	270 (36.99%)	460 (63.01%)	730	-	-	-
octogenarian	414 (50.92%)	399 (49.08%)	813 (100%)	-	-	-	414 (50.92%)	399 (49.08%)	813	-	-	-
Younger elderly	537 (62.22%)	326 (37.78%)	863 (100%)	-	-	-	537 (62.22%)	326 (37.78%)	863	-	-	-
2012 follow-up	518 (41.27%)	737 (58.73%)	1255 (31.65%)	1165 (42.99%)	1545 (57.01%)	2710 (68.35%)	1683 (42.45%)	2282 (57.55%)	3965	377 (34.81%)	706 (65.19%)	1083 (27.31%)
centenarian	62 (14.90%)	354 (85.1%)	416 (40.74%)	85 (14.05%)	520 (85.95%)	605 (59.26%)	147 (14.40%)	874 (85.60%)	1021	61 (13.96%)	376 (86.04%)	437 (42.80%)
nonagenarian	96 (40.68%)	140 (59.32%)	236 (26.85%)	243 (37.79%)	400 (62.21%)	643 (73.15%)	339 (38.57%)	540 (61.43%)	879	144 (39.67%)	219 (60.33%)	363 (41.30%)
octogenarian	147 (52.50%)	133 (47.5%)	280 (28.48%)	362 (51.49%)	341 (48.51%)	703 (71.52%)	509 (51.78%)	474 (48.22%)	983	122 (58.37%)	87 (41.63%)	209 (21.26%)
Younger elderly	213 (65.94%)	110 (34.06%)	323 (29.85%)	475 (62.58%)	284 (37.42%)	759 (70.15%)	688 (63.59%)	394 (36.41%)	1082	50 (67.57%)	24 (32.43%)	74 (6.84%)
2014 follow-up	390 (42.39%)	530 (57.61%)	920 (18.86%)	1651 (41.71%)	2,307 (58.29%)	3958 (81.14%)	2041 (41.84%)	2837 (58.16%)	4878	380 (55.07%)	310 (44.93%)	690 (14.15%)

centenarian	34 (16.59%)	171 (83.41%)	205 (16.76%)	142 (13.95%)	876 (86.05%)	1018 (83.24%)	176 (14.39%)	1,047 (85.61%)	1223	107 (41.00%)	154 (59.00%)	261 (21.34%)
nonagenarian	124 (42.61%)	167 (57.39%)	291 (24.37%)	344 (38.10%)	559 (61.90%)	903 (75.63%)	468 (39.20%)	726 (60.80%)	1194	90 (44.33%)	113 (55.67%)	203 (17.00%)
octogenarian	116 (45.85%)	137 (54.15%)	253 (20.16%)	517 (51.60%)	485 (48.40%)	1002 (79.84%)	633 (50.44%)	622 (49.56%)	1255	104 (63.03%)	61 (36.97%)	165 (13.15%)
Younger elderly	116 (67.84%)	55 (32.16%)	171 (14.18%)	648 (62.61%)	387 (37.39%)	1035 (85.82%)	764 (63.35%)	442 (36.65%)	1206	41 (67.21%)	20 (32.79%)	61 (5.06%)
2017 follow-up	601 (42.50%)	813 (57.5%)	1414 (37.96%)	1026 (44.40%)	1,285 (55.60%)	2311 (62.04%)	1627 (43.68%)	2098 (56.32%)	3725	309 (36.74%)	532 (63.26%)	841 (22.58%)
centenarian	58 (17.26%)	278 (82.74%)	336 (42.21%)	77 (16.74%)	383 (83.26%)	460 (57.79%)	135 (16.96%)	661 (83.04%)	796	57 (17.48%)	269 (82.52%)	326 (40.95%)
nonagenarian	151 (49.19%)	156 (50.81%)	307 (35.78%)	222 (40.29%)	329 (59.71%)	551 (64.22%)	373 (43.47%)	485 (56.53%)	858	120 (41.96%)	166 (58.04%)	286 (33.33%)
octogenarian	127 (51.00%)	122 (49.00%)	249 (28.20%)	298 (47.00%)	336 (53.00%)	634 (71.80%)	425 (48.13%)	458 (51.87%)	883	91 (52.30%)	83 (47.70%)	174 (19.71%)
Younger elderly	265 (50.77%)	257 (49.23%)	522 (43.94%)	429 (64.41%)	237 (35.59%)	666 (56.06%)	694 (58.42%)	494 (51.87%)	1188	41 (74.55%)	14 (25.45%)	55 (4.63%)

Table 2. Baseline characteristics of HABCS participants.

	Younger elderly	Octogenarians	Nonagenarians	Centenarians
No. of participants	1,879	1,564	1,595	1,635
Age, median, y	72 (68-75)	84 (82-87)	93 (91-95)	101 (100-102)
Female	743 (39.73%)	785 (49.43%)	922 (59.03%)	1,382 (85.10%)
BMI, kg/m^2	22.68 (20.32-25.00)	20.76 (18.42-23.45)	19.84 (17.67-22.31)	19.02 (16.89-21.43)
Rural residence	1,422 (76.00%)	1,188 (74.81%)	1,167 (74.71%)	1,264 (77.78%)
Education time ≥ 1	1,228 (65.63%)	536 (33.75%)	337 (21.57%)	161 (9.91%)
Married	1,403 (74.99%)	675 (42.51%)	257 (16.45%)	54 (3.32)
Smoking	522 (27.90%)	319 (20.09%)	240 (15.36%)	109 (6.71%)
Drinking	445 (23.78%)	287 (18.07%)	239 (15.30%)	180 (11.08%)
Exercise at present	532 (28.43%)	334 (21.03%)	260 (16.65%)	169 (10.40%)
Hypertension	515 (27.53%)	417 (26.26%)	360 (23.05%)	259 (15.94%)
Diabetes mellitus	100 (5.34%)	45 (2.83%)	24 (1.54%)	8 (0.49%)
Heart disease	181 (9.67%)	127 (8.00%)	96 (6.15%)	75 (4.62%)
Stroke/CVD	104 (5.56%)	127 (8.00%)	79 (5.06%)	88 (5.42%)
Respiratory disease	175 (9.35%)	177 (11.15%)	141 (9.03%)	120 (7.38%)

Continuous variables are expressed as medians and interquartile ranges; categorical variables were expressed as frequencies (percentages).

Abbreviations: BMI, body mass index; CVD, cardiovascular disease

Table 3. Data Collection from *Questionnaire for Interviews to the Surviving Participants* in HABCS.

Questionnaire for Interviews to the Surviving Participants in HABCS		
Basic Information	**Life Evaluation and Personality**	**Mini Mental State Examination (MMSE)**
Sex	Life Satisfaction and Self-Rated Health	Orientation
Ethnic group	Personality	Registration
Age		Attention and Calculation
Place of Birth		Recall
Characteristics of Current Residence		Language
Life Style	**Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL)**	**Personal Background**
Diet	Limited in Activities	Education
Smoke	ADL	Primary Occupation before age 60
1.Tobacco-Nicotine Dependence	Bathing	Retirement Age
2.Personal Perception and Knowledge of Smoking-related Cancer Risk	Dressing	Pension for Retirement
	Toilet	Public Old Age Insurance
	Indoor Transfer	Financial Support
	Continence	Economic Status
	Eating	Current Marital Status
3.Passive Smoke Exposure	Characteristics of Caregiver	Medical Service
Alcohol	IADL	Social Security and Commercialized Insurances
Alcohol - Lifetime Abuse and Dependence	Cleaning	Childhood status
	Managing money	Mother's Information
Exercises	Moving within the community	Father's Information
Physical Activity	Preparing meals	Birth Order
Other Activities	Shopping	Biological Brothers' and Sisters' Information
	Taking prescribed medications	Children's Information
	Using the telephone	Money Gotten/Given
		Social Services in The Living Community
		Preference of Living Arrangement
Objective Examination and Illnesses Attention		
Sleep Quality		
Teeth Status		

Oral Hygiene of Personal Care
Toothache and Orofacial Pain
Hand Dominance
Standing Height or
Self-Reported Height
Waist Circumference
Hearing loss
Physical Illnesses

Table 4. Biological samples tested in HABCS.

Biological Samples	**Specific Biological Indicators Tested**
Blood Routine Examination	Blood platelet, Hemoglobin, Red Blood Cell, White blood cell
Urine Routine Examination	Bilirubin, Creatinine, Erythrocyte, Glucose, Ketone body, Leukocyte, Microalbuminuria, Nitrite, Occult blood, Specific gravity, Urine protein, Urobilinogen, pH,
Blood Biochemistry	Fasting blood-glucose, Glycated albumin, High-density lipoprotein, High-sensitivity C-reactive protein, Low density lipoprotein, Malondialdehyde, Plasma albumin, Serum creatinine, Superoxide dismutase, Total cholesterol, Triglyceride, Uric acid, Urea nitrogen, 25-Hydroxyvitamin D

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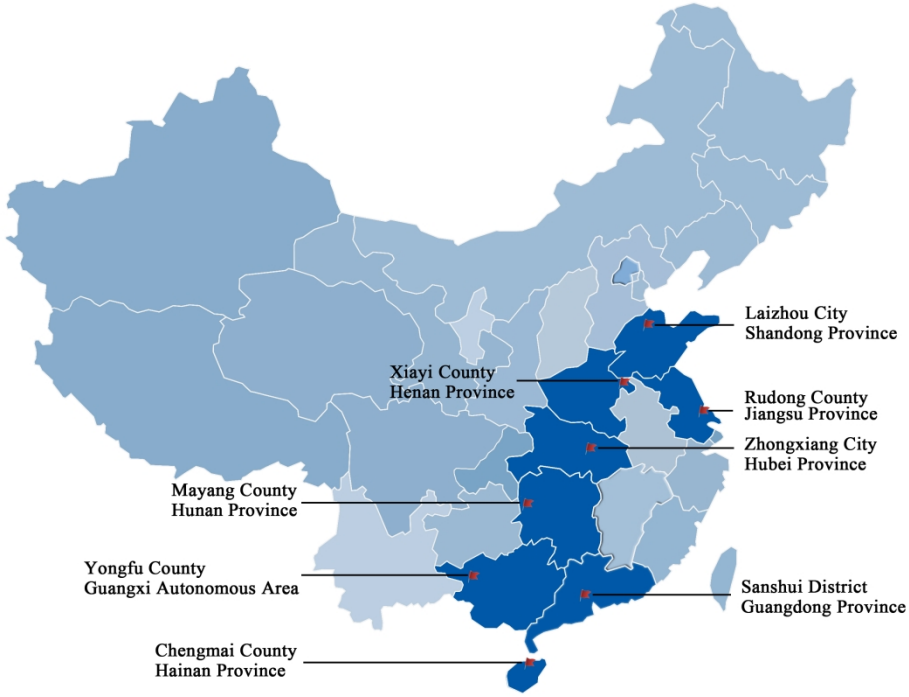
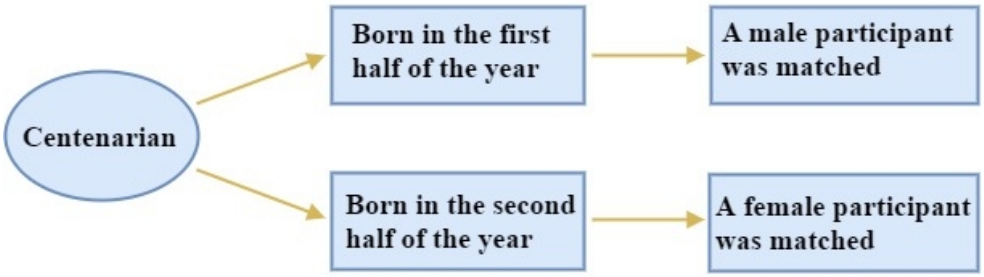


Figure 1. Selected longevity areas in China for sampling in HABCS.

1058x811mm (72 x 72 DPI)



219x64mm (72 x 72 DPI)